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EXAMINER	
CHEN, LIPING	
ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/869,508	Applicant(s) DORKEN ET AL.	
	Examiner Liping Chen	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *4 and 5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06/05/2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

Lack of unity is required under 35 U.S.C. 121 and 372. This application contains the following inventions or goups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

I. Claims 1-3 and 6-10, drawn to a gene transfer vector comprising the YB-1 promoter, its mutants, or deletion variants, and a reporter gene.

II. Claims 1,2, 4 in part, and 6-10, drawn to a gene transfer vector comprising the YB-1 promoter, its mutants, or deletion variants, and a cell-cycle regulating gene.

III. Claims 1, 2, 4 in part, and 6-10, drawn to a gene transfer vector comprising the YB-1 promoter, its mutants, or deletion variants, and a proapoptotic gene.

IV. Claims 1, 2 and 5-10, drawn to a gene transfer vector comprising the YB-1 promoter, its mutants, or deletion variants, and a tumor suppressor gene or an apoptotic gene.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Group I

encompasses to a gene transfer vector comprising a reporter gene. Groups II-IV are directed to different gene transfer vectors comprising different genes: cell-cycle regulating gene, proapoptotic gene, and a tumor suppressor gene or an apoptotic gene, respectively, which represent different special technical features. Further, 37 CFR 1.475 does not provide for multiple independent products, methods of manufacture and methods of use (37 CFR 1.475(d). Therefore, The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1.

Status of the claims

A restriction was made on 10/01/2002. Applicant's election with traverse of Group I, claims 1-3 and 6-10, drawn to a gene transfer vector comprising the YB-1 promoter, its mutants, or deletion variants and a reporter gene, in Paper No. 5, is acknowledged. The traversal is on the ground(s) that the examiner has applied an incorrect legal standard for determining whether restriction is appropriate. This is not found persuasive because the reasons described above. Thus, the requirement is still deemed proper and is therefore made FINAL. Therefore, only Group I is examined in this office action.

Claims 4 and 5 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invenstion, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10.

Claims 1-10 are pending and claims 1-3 and 6-10 are under current consideration.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 12/29/1998. It is noted, however, that applicant has not filed a certified English Translation copy of the Germany application as required by 35 U.S.C. 119(b).

Claim Objection

Claim 1 is objected to for using bullets; it is suggested using letters A, B, C etc or i, ii, iii, etc instead.

Specification

The disclosure is objected to because of the following informalities:

The description of the drawings for Fig. 2 is objected to because it is not clear what is meant by a "box-of-bricks" system. There is no definition in the specification.

Page 6, first parag., states "results a kind of 'box-of-bricks' system". There is no definition as what kind of system is a "box-of-bricks" system in the specification.

Fig. 4 is objected because it does not distinguish A2 from A3 or B2 from B3.

Claim Rejections - 35 USC § 112, 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, as written is indefinite, as using the phrase "suited to cutting out the transgene for restriction enzymes surrounding the transgene". It is not clear how restriction enzymes surround the transgene.

Claim 8, as written are indefinite as using the term of "for restriction enzymes 5-10". It is not clear what "5-10" indicates.

Claim Rejections - 35 USC § 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 6-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to a gene transfer vector comprising the YB-1 promoter, its mutants or deletion variants; a transgene or the cDNA of a transgene, two multi-cloning sites (MCS) suited to cutting out the transgene for restriction enzymes surrounding the transgene; claim 2 and 3 are directed to the gene transfer vector of claim 1 comprising a specific transgene; claims 6 is directed to the gene transfer vector of claim 1, wherein a regulating element is additionally inserted into the vector; claims 7 and 8 are directed to the gene transfer vector of claim 1, wherein MCS contain at least 3 enzyme restriction sites; claim 9 is directed to the gene transfer vector of claim 1, wherein the multi-cloning sites for restriction enzymes contain no enzyme restriction sites occurring within the sequences of the YB-1 promoter; claim 10 is directed to the gene transfer vector of claim 1, wherein the MCS contain sticky and blunt enzyme restriction sites for restriction enzyme.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does

not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, while a written description for using pCR2.1 vector of Invitrogen and nucleotide 453-2150 of the YB-1 promoter sequence of GenBank accession No. X96666 (specification, page 6) to construct a gene transfer vector is generally understood, there is no written description regarding the chemical structure of YB-1 promoter mutants or deletion variants that having YB-1 promoter activity, no written description regarding the structure feature of the gene transfer vectors claimed, such as the relationship among promoter, transgene and MCS, and what kind of regulating elements (pertaining to instant claim 6) are included for vector construction and the position of an additionally inserted regulating element in a vector. Claim 9 specifically points out that MCS do not contain restriction enzyme sites occurring within the sequences of the YB-1 promoter, however, there is no written description regarding the restriction enzyme sites existing within YB-1 promoter. Therefore, with the exception of using nucleotide 453-2150 of the YB-1 promoter sequence of GenBank accession No. X96666 and pCR2.1 vector of Invitrogen for gene transfer vector construction, the skilled artisan cannot envision the detailed chemical structure of a gene transfer vector comprising YB-1 promoter or its mutants or deletion variants and the restriction enzyme sites that exist in MCS of the vector. Further, the skilled artisan cannot envision what kind of additional regulatory element is included in the vector, such as a regulatory

element for activation of YB-1 promoter or suppression of YB-1 promoter, or a regulatory element that is another promoter for a different transgene expression. It is noted that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, only a gene transfer vector is derived from pCR2.1 vector of Invitrogen and containing nucleotide 453-2150 of the YB-1 promoter sequence of GenBank accession No. X96666, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated Makino et al. (Nucleic Acids Res. 24:1873-1878, 1996).

Claim 1 is directed to a gene transfer vector comprising the YB-1 promoter, its mutants or deletion variants; a transgene or the cDNA of a transgene, two multi-cloning sites (MCS) suited to cutting out the transgene for restriction enzymes surrounding the transgene; claim 2 and 3 are further directed to the gene transfer vector of claim 1 comprising a specific transgene such as a therapeutic gene (claim 2), or a reporter gene (claim 3); claims 6 is directed to the gene transfer vector of claim 1, wherein a regulating element is additionally inserted into the vector.

Makino et al. teach to use pSVOOCAT reporter vector for testing YB-1 gene promoter activity using different fragments of the 5'-end untranslated region of YB-1 gene (Makino, Abstract, page 1874, left col., and Fig. 3). The pSVOOCAT reporter plasmid [containing different fragment of YB-1 promoter taught by Makino et al.] is a gene transfer vector comprising a YB-1 promoter and reporter gene, which can be

cut out by HindIII and BamHI as evidenced by Araki (see page 1627). As there is no definition as what kind of gene is therapeutic gene, the vector taught by Makino et al. also meets the limitation of claim 2. Moreover, the origin of replication and ampicillin resistance genes of pBR322 in the pSVOCAT vector remained in the pSVOOCAT vector (see Araki, page 1627 and Gorman, page 1045, right col.), and anticipate the regulation limitation of claim 6. Thus, Makino et al. clearly anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Makino et al. (Nucleic Acids Res. 24:1873-1878, 1996) in view of Araki et al. (Nucleic Acids Res. 16:1627, 1988) and Gorman et al. (Mol Cell Biol 2:1044-1051, 1988), further in view of Pharmacia Biotech Catalog (Pharmacia Biotech, page 121-126, 1995).

Claim 1 is directed to a gene transfer vector comprising the YB-1 promoter, its mutants or deletion variants; a transgene or the cDNA of a transgene, two multi-cloning sites (MCS) suited to cutting out the transgene for restriction enzymes surrounding the transgene; claims 7 and 8 are directed to the gene transfer vector of claim 1, wherein MCS contain at least 3 enzyme restriction sites; claim 9 is directed to the gene transfer vector of claim 1, wherein the multi-cloning sites for restriction enzymes contain no enzyme restriction sites occurring within the sequences of the YB-1 promoter; claim 10 is directed to the gene transfer vector of claim 1, wherein the MCS contain sticky enzyme and blunt enzyme restriction sites.

Makino et al. teach to use pSVOOCAT reporter vector for testing YB-1 gene promoter activity using different fragments of the 5'-end untranslated region of YB-1 gene (Makino, Abstract, page 1874, left col., and Fig. 3). Makino et al. state that deletion of –119 to +24 of YB-1 gene diminished promoter activity by ~45% (Makino, page 1875, right col.). The pSVOOCAT reporter plasmid containing different fragment of YB-1 promoter taught by Makino et al. is a gene transfer vector comprising YB-1 promoter and reporter gene, which can be cut out by HindIII and BamHI in view of pSVOOCAT vector construction (Araki, page 1627), which is derived from pSVOCAT (Gorman, page 1045, right col. Fig. 1, page 1047, right col., page 1048, left col. and Fig 3). In the construction of pSVOCAT, Gorman et al. teach to use HindIII and BamHI sites for foreign polypeptide coding sequences

insertion (Gorman, page 1045, right col.). However, Gorman et al. does not teach to use MCS for foreign polypeptide coding sequences insertion.

However, at the time the claimed invention was made, methods of constructing and using MCS for insertion of transgene were within the routine skill of the ordinary artisan as evidenced by Pharmacia Biotech Catalog (Pharmacia Biotech, page 121-126). One of ordinary skill in the art would have been sufficiently motivated to add MCS in the transgene insertion region to simplify insertion of different transgene with a reasonable expectation of success. The restriction sites used in MCS can be selected from common used restriction enzyme sites such as MCS contained in pUC18 used by Makino et al. (Makino, page 1874, right col. last parag.), which contain SmaI and HincII as blunt ended and Hind III and other 9 sticky ended restriction enzyme sites (Pharmacia, page 126), or select any restriction sites designed (pertaining to instant claim 9).

Thus, the claimed invention, as a whole, was clearly prima facie obvious in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Liping Chen, whose telephone number is (703)

305-4842. The examiner can normally be reached on Monday through Friday from 8:00 to 5:00 (Eastern Standard Time). Should the examiner be unavailable, inquiries should be directed to Deborah Reynolds, Supervisory Primary Examiner of Art Unit 1632, at (703) 305-4051. Any administrative or procedural questions should be directed to Dianiece Jacobs, Patent Analyst, at (703) 305-3550. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-8724.

Liping Chen, Ph.D.
Patent Examiner
Group 1632

Art Unit 1632